

claims 1, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14 and 15 to more fully conform with U.S. practice and to delete multiple dependencies. Applicants have also added new claims 16 and 17. A version of the claims marked up to show the amendments, as well as a clean version of the claims encompassing the amendments, is attached hereto.

Applicants respectfully assert that all amendments are fairly based on the specification, and respectfully request their entry.

Applicants believe that the claims, as amended, are in allowable form, and earnestly solicit the allowance of claims 1-17.

Respectfully submitted,



Royal N. Ronning, Jr. 32,529  
Attorney for Applicants

Amersham Pharmacia Biotech, Inc.  
800 Centennial Avenue  
P. O. Box 1327  
Piscataway, New Jersey 08855-1327

Tel: (732) 457-8423  
Fax: (732) 457-8463

## Claims (marked-up version showing amendment(s))

Page 13, line 1:

### [CLAIMS]

What is claimed is:

1. (once amended) A method of detecting and analysing differences between nucleic acids from two sources, which method comprises:
  - a. providing the nucleic acids from two sources as labelled probes wherein the nucleic acids from two sources are labelled with two different markers;
  - b. forming a mixture of the labelled probes with pooled reagents wherein each of the pooled reagents comprises[reagent is] a population of beads carrying a polynucleotide target, the polynucleotide target of any one of the pooled reagents[reagent] being different from the target of [another reagent,]any other of the pooled reagents and the beads of any one of the pooled reagents[reagent] being distinguishable from the beads of [another reagent]any other of the pooled reagents;
  - c. incubating the mixture under conditions to promote specific hybridisation between probes and targets; and
  - d. analysing beads in the mixture by flow cytometry.

3. (once amended) The method of claim 1[ or claim 2] wherein the polynucleotide targets are cDNA derived from cellular mRNA.
4. (once amended) The method of [any one of claims 1 to 3]claim 1 wherein the polynucleotide targets are PCR amplimers.
5. (once amended) The method of [any one of claims 1 to 4]claim 1 wherein the polynucleotide targets [carry]contain terminal biotin groups through which they are attached to streptavidin-coated beads.
6. (once amended) The method of [any one of claims 1 to 5]claim 1 wherein the polynucleotide targets are single-stranded nucleic acids.
7. (once amended) The method of [any one of claims 1 to 6]claim 1 wherein the [labelled probes]nucleic acids are single-stranded nucleic acids.
8. (once amended) The method of [any one of claims 1 to 7]claim 1 wherein beads of one pooled reagent are distinguishable from beads of another pooled reagent by size.
9. (once amended) The method of [any one of claims 1 to 8]claim 1 wherein beads

of one pooled reagent are distinguishable from beads of another pooled reagent by the nature of [the] one or more markers attached to the beads.

10. (once amended) The method of [any one of claims 1 to 9] claim 1 wherein beads of one pooled reagent are distinguishable from beads of another pooled reagent by the concentration of one or more markers attached to the beads.
11. (once amended) The method of [any one of claims 1 to 7] claim 1 wherein beads of one pooled reagent are distinguishable from beads of another pooled reagent by the size and/or by the nature [and/or] and the concentration of one or more markers attached to the beads.
12. (once amended) The method of [any one of claims 8 to 11] claim 9 wherein the markers are fluorescent markers [are ] attached to the beads.
13. (once amended) The method of claim 1 [ or claim 2] wherein each [probe] of the nucleic acids is labelled with a fluorescent tag to indicate its source.
14. (once amended) The method of [any one of claims 1 to 13] claim 1 wherein the analysis by flow cytometry is performed to identify each bead and to quantify the probes bound thereto.

15. (once amended) The method of [any one of claims 1 to 14]claim 1  
[wherein]further comprising the step of analysing the data obtained by flow  
cytometry [is analysed ]to yield information about the relative and/or absolute  
abundances of individual nucleic acid sequences [of]contained within the nucleic  
acids from [the ]two sources.
16. (new) The method of claim 10 wherein the markers are fluorescent markers  
attached to the beads.
17. (new) The method of claim 11 wherein the markers are fluorescent markers  
attached to the beads.